

SEQUENCE LISTING

<110> DAVIS, SIMON

<120> RECEPTOR MODULATORS

<130> ISI.103

<140> US 10/585,491

<141> 2006-07-07

<150> PCT/GB05/000099

<151> 2005-01-10

<150> GB 0400440.4

<151> 2004-01-09

<150> US 60/536,354

<151> 2004-01-14

<160> 61

<170> PatentIn version 3.2

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<212> PRT

<213> Homo sapiens

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<223> HUMAN CD28

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Met Leu Arg Leu Leu Leu Ala Leu Asn Leu Phe Pro Ser Ile Gln Val
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Thr Gly Asn Lys Ile Leu Val Lys Gln Ser Pro Met Leu Val Ala Tyr
20 25 30

Asp Asn Ala Val Asn Leu Ser Cys Lys Tyr Ser Tyr Asn Leu Phe Ser
35 40 45

Arg Glu Phe Arg Ala Ser Leu His Lys Gly Leu Asp Ser Ala Val Glu
50 55 60

Val Cys Val Val Tyr Gly Asn Tyr Ser Gln Gln Leu Gln Val Tyr Ser
65 70 75 80

Lys Thr Gly Phe Asn Cys Asp Gly Lys Leu Gly Asn Glu Ser Val Thr
85 90 95

Phe Tyr Leu Gln Asn Leu Tyr Val Asn Gln Thr Asp Ile Tyr Phe Cys
100 105 110

Lys Ile Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser
 115 120 125

Asn Gly Thr Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro
 130 135 140

Leu Phe Pro Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly
 145 150 155 160

Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile
 165 170 175

Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met
 180 185 190

Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro
 195 200 205

Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
 210 215 220

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<223> CD28/Fc fusion protein

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Ile Asn Ala Asn Lys Ile Leu Val Lys Gln Ser Pro Met Leu Val Ala
 20 25 30

Tyr Asp Asn Ala Val Asn Leu Ser Cys Lys Tyr Ser Tyr Asn Leu Phe
 35 40 45

Ser Arg Glu Phe Arg Ala Ser Leu His Lys Gly Leu Asp Ser Ala Val
 50 55 60

Glu Val Cys Val Val Tyr Gly Asn Tyr Ser Gln Gln Leu Gln Val Tyr
 65 70 75 80

Ser Lys Thr Gly Phe Asn Cys Asp Gly Lys Leu Gly Asn Glu Ser Val
 85 90 95

Thr Phe Tyr Leu Gln Asn Leu Tyr Val Asn Gln Thr Asp Ile Tyr Phe
 100 105 110

Cys Lys Ile Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys

115	120	125
Ser Asn Gly Thr Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser		
130	135	140
Pro Leu Phe Pro Gly Pro Ser Lys Pro Leu Val Pro Arg Gly Ser Gly		
145	150	155
Ser Lys Pro Ser Ile Ser Thr Val Pro Glu Val Ser Ser Val Phe Ile		
	165	170
		175
Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys		
	180	185
		190
Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln		
	195	200
		205
Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln		
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Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu		
	225	230
		235
Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg		
	245	250
		255
Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys		
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		270
Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro		
	275	280
		285
Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr		
	290	295
		300
Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln		
	305	310
		315
Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly		
	325	330
		335
Ser Tyr Phe Val Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu		
	340	345
		350
Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn		
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His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys		
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Xaa
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<210> 12
 <211> 31
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<210> 13
 <211> 31
 <212> DNA
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<400> 13
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<210> 14
 <211> 34
 <212> DNA
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<223> OLIGONUCLEOTIDE PRIMER

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ctactatcta gattatttac caggagagtg ggag

34

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<211> 1514

<212> DNA

<213> Homo sapiens

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ctcaacttat tcccttcaat tcaagtaaca ggaaacaaga ttttggtgaa gcagtcgccc	180
atgcttgtag cgtacgacaa tgcggtaaac cttagctgca agtattccta caatctcttc	240
tcaagggagt tccgggcata ctttcacaaa ggactggata gtgctgtgga agtctgtgtt	300
gtatatggga attactccca gcagcttcag gtttactcaa aaacgggggt caactgtgat	360
gggaaattgg gcaatgaata agtgacattc tacctccaga atttgtatgt taaccaaaaca	420
gatatttact tctgcaaaat tgaagttatg tatectcttc cttacctaga caatgagaag	480
agcaatggaa ccattatcca tgtgaaaggg aaacaccttt gtccaagtc cctatttccc	540
ggaccttcta agcccttttg ggtgctggtg gtgggtgggt gagtcctggc ttgctatagc	600
ttgctagtaa cagtggcctt tattattttc tgggtgagga gtaagaggag caggctcctg	660
cacagtgact acatgaacat gactccccgc cggcccgggc ccaccgcaa gcattaccag	720
ccctatgccc caccacgaga cttcgcagcc tategtcctt gacacggacg cctatccaga	780
agccagccgg ctggcagccc ccattctgctc aatatactg ctctggatag gaaatgaccg	840
ccatctccag ccggccacct cagccctgtt tgggcccaca atgccaat tctctgagtg	900
actagaccaa atatcaagat ctttttgaga ctctgaaatg aagtaaaaga gatttcctgt	960
gacaggccaa gtcttacagt gccatggccc acattccaac ttaccatgta cttagtgaat	1020
tgaactgaaa gttagggtag aaaacaaaaa gggagtggat tctgggagcc tcttcccttt	1080
ctcaactcac tgcacatctc agtcaagcaa agtgtggtat ccacagacat tttagttgca	1140

gaagaaaggc taggaaatca ttcccttttgg ttaaatgggt gtttaattctt ttggtttagtg 1200
 gggttaaacgg ggtaagttag agtaggggga gggataggaa gacatattta aaaaccatta 1260
 aaacactgtc tcccactcat gaaatgagcc acgtagtctc tatttaaatgc tgttttccctt 1320
 tagtttagaa atacatagac attgtctttt atgaattctg atcatattta gtcattttga 1380
 ccaaattgagg gatttggtea aatgagggat tccctcaaag caatatcagg taaaccaagt 1440
 tgctttctct actccctgtc atgagacttc agtgtaaatg ttcacaatat acttttcgaaa 1500
 gaataaaata gttc 1514

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 gccgctcaaa gtatcaacgc gaacaagatc ttggtgaagc agtcgcccac gcttgtagcg 120
 taogacaatg cggteaacct tagctgcaag tattcctaca atctcttctc aaggaggctc 180
 cgggcacccc ttcacaaagg actggatagt gctgtggaag tctgtgttgt atatgggaat 240
 tactcccagc agcttcaggt ttactcaaaa acgggggttc actgtgatgg gaaattgggc 300
 aatgaatcag tgacattcta cctccagaat ttgtatgtta accaaacaga tatttaactc 360
 tgcaaaattg aagttatgta tctctctct taactagaca atgagaagag caatgggtacc 420
 attatccatg tgaaagggaa acacctttgt ccaagtcgcg tatttcccg accctctaag 480
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 tctgtcttca tcttcccccc aaagoccaaag gatgtgctca ccattactct gactcctaag 600
 gtcagtggtg ttgtggtaga catcagcaag gatgatcccg aggtccagtt cagctgggtt 660
 gtagatgatg tggaggtgca cacagctcag acgcaacccc gggaggagca gttcaacagc 720
 actttccgct cagtcagtga acttcccatc atgcaccagg actggctcaa tggcaaggag 780
 ttcaaattgca gggteaacag tgcagcttcc cctgcoccca tcgagaaaac catctccaaa 840
 accaaaggca gaccgaaggc tccacaggtg tacaccatc cacctcccaa ggagcagatg 900
 gccaaagata aagtcagttc gacctgcag ataacagact tcttccctga agacattact 960

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gtggagtggc agtggaatgg gcagccagcg gagaactaca agaactca gccatcatg 1020
gacacagatg gctcttactt cgtctacagc aagctcaatg tgcagaagag caactgggag 1080
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<210> 17
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Ile Ala Ser Phe Val Cys Glu Tyr Ala Ser Pro Gly Lys Ala Thr Glu
          20          25          30

Val Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val
          35          40          45

Cys Ala Ala Thr Tyr Met Met Gly Asn Glu Leu Thr Phe Leu Asp Asp
          50          55          60

Ser Ile Cys Thr Gly Thr Ser Ser Gly Asn Gln Val Asn Leu Thr Ile
65          70          75          80

Gln Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu
          85          90          95

Leu Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln
          100          105          110

Ile Tyr Val
          115

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<223> HUMAN ICOS

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Glu Ile Asn Gly Ser Ala Asn Tyr Glu Met Phe Ile Phe His Asn Gly
1           5           10           15

Gly Val Gln Ile Leu Cys Lys Tyr Pro Asp Ile Val Gln Gln Phe Lys
           20           25           30

Met Gln Leu Leu Lys Gly Gly Gln Ile Leu Cys Asp Leu Thr Lys Thr
           35           40           45

Lys Gly Ser Gly Asn Thr Val Ser Ile Lys Ser Leu Lys Phe Cys His
50           55           60

Ser Gln Leu Ser Asn Asn Ser Val Ser Phe Phe Leu Tyr Asn Leu Asp
65           70           75           80

His Ser His Ala Asn Tyr Tyr Phe Cys Asn Leu Ser Ile Phe Asp Pro
           85           90           95

Pro Pro Phe Lys Val Thr Leu Thr Gly Gly Tyr Leu His Ile
           100          105          110

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<223> HUMAN PD-1

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Pro Pro Thr Phe Phe Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn
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Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu
           20           25           30

Asn Trp Tyr Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala
           35           40           45

Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val
50           55           60

Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala
65           70           75           80

Arg Arg Asn Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala
           85           90           95

Pro Lys Ala Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg

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100

105

110

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 Val Thr Phe Thr Cys Arg Ser Ser Gln Thr Ile Gly Thr Tyr Leu Asn
 20 25 30
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Lys Leu Leu Ile Phe Ala
 35 40 45
 Ala Ser Ser Leu Leu Asn Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
 50 55 60
 Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
 65 70 75 80
 Phe Ala Thr Tyr Tyr Cys Gln Gln Ser His Ser Ala Pro Pro Tyr Thr
 85 90 95
 Phe Gly Gln Gly Thr Arg Leu Glu Met Lys
 100 105

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 Ser Thr Leu Arg Cys Asn Phe Ser Asp Ser Val Asn Asn Leu Gln Trp
 20 25 30
 Phe His Gln Asn Pro Trp Gly Gln Leu Ile Asn Leu Phe Tyr Ile Pro
 35 40 45

Ser Gly Thr Lys Gln Asn Gly Arg Leu Ser Ala Thr Thr Val Ala Thr
50 55 60

Glu Arg Tyr Ser Leu Leu Tyr Ile Ser Ser Ser Gln Thr Thr Asp Ser
65 70 75 80

Gly Val Tyr Phe Cys Ala Ala Leu Asp Leu Trp Gly Gly Ala Asp Gly
85 90 95

Leu Thr Phe Gly Lys Gly Thr His Leu Ile Ile Gln
100 105

<210> 22
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<223> HUMAN BTLA

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Gln Leu Tyr Ile Lys Arg Gln Ser Glu His Ser Ile Leu Ala Gly Asp
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Pro Phe Glu Leu Glu Cys Pro Val Lys Tyr Cys Ala Asn Arg Pro His
20 25 30

Val Thr Trp Cys Lys Leu Asn Gly Thr Thr Cys Val Lys Leu Glu Asp
35 40 45

Arg Gln Thr Ser Trp Lys Glu Glu Lys Asn Ile Ser Phe Phe Ile Leu
50 55 60

His Phe Glu Pro Met Leu Pro Asn Asp Asn Gly Ser Tyr Arg Cys Ser
65 70 75 80

Ala Asn Phe Gln Ser Asn Leu Ile Glu Ser His Ser Thr Thr Leu Tyr
85 90 95

Val Thr

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<400> 23

Ser Pro Met Leu Val
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<210> 24
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<400> 24

Pro Ala Val Val Leu
1 5

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Tyr Glu Met Phe Ile
1 5

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Ala Val Asn Leu Ser
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Gly Ile Ala Ser Phe Val
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Gly Val Gln Ile Leu
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Ser Leu His Lys Gly Leu Asp Ser Ala Val Glu Val Cys Val
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Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys Ala
1 5 10 15

<210> 31

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<212> PRT

<213> Artificial sequence

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Gln Leu Leu Lys Gly Gly Gln Ile Leu Cys Asp
1 5 10

<210> 32

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<212> PRT

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<223> hCD28 epitope

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Val Tyr Ser Lys Thr Gly Phe Asn Cys Asp Gly
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<210> 33

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<212> PRT

<213> Artificial sequence

<220>

<223> hCTLA-4 epitope

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Phe Leu Asp Asp Ser Ile Cys Thr Gly
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Val Ser Ile Lys Ser Leu Lys Phe Cys His Ser
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<400> 35

Phe Tyr Leu Gln Asn
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Leu Thr Ile Gln Gly
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Pro Ala Leu Leu Val Val
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Gln Ser Glu His Ser Ile
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Asp Asn Ala Thr Phe
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Asp Pro Phe Glu Leu
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Arg Met Ser Pro Ser Asn Gln Thr Asp Lys
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Lys Leu Asn Gly
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Gln Pro Gly Gln Asp Cys Arg Phe Arg
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Gln Thr Ser Trp Lys
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Met Ser Val Val Arg
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Leu His Phe Glu Pro
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Asn Asp Ser Gly Thr Tyr
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Asn Asp Asn Gly Ser Tyr
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Leu Arg Ala Glu Leu Arg
 1 5

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Thr Thr Leu Tyr Val Thr
 1 5

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Tyr Met Met Gly Asn Glu Leu Thr Phe Leu Asp Asp Ser
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Lys Thr Lys Gly Ser Gly Asn Thr Val Ser Ile Lys Ser Leu Lys
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Leu Ala Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg
 1 5 10 15